510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

k081360

B. Purpose for Submission:

New device.

C. Measurand:

Creatine Kinase MB (CK-MB) and Myoglobin

D. Type of Test:

Quantitative

E. Applicant:

Mitsubishi Kagaku Iatron Inc.

F. Proprietary and Established Names:

PATHFAST© CK-MB-II

PATHFAST© Myo-II

PATHFAST CK-MB Calibrator

PATHFAST Myo Calibrator

G. Regulatory Information:

1. Regulation section:

   21 CFR 862.1215 Creatine Phosphokinase/creatine kinase or isoenzymes test system (CK-MB)

   21 CFR 866.5680 Myoglobin immunological test system

   2 CFR 862.1150 Calibrator, secondary

2. Classification:

   Class II (All three)

3. Product code:

   JHX, DDR, JIT respectively.

4. Panel:

   75 (Chemistry), 81 (Hematology) and 75 (Chemistry) respectively.

H. Intended Use:

1. Intended use(s):

   See indications for use statement below.

2. Indication(s) for use:
   PATHFAST CK-MB-II test is an in vitro diagnostic test for the quantitative measurement of creatine kinase-MB in heparinized or EDTA whole blood and plasma. Measurements of CK-MB are used in the diagnosis of acute myocardial infarction (MI). This method is for use in clinical laboratory or point of care (POC) settings.

   The PATHFAST CK-MB Calibrators are for calibration for the PATHFAST system when used for the quantitative determination of creatine kinase-MB in human heparinized or EDTA whole blood and plasma.

   PATHFAST Myo-II test is an in vitro diagnostic test for the quantitative measurement of myoglobin in heparinized or EDTA whole blood and plasma. Measurements of myoglobin are used in the diagnosis of acute myocardial infarction (MI). This method is for use in clinical laboratory or point of care (POC) settings.

   The PATHFAST Myo Calibrators are for calibration for the PATHFAST system when used for the quantitative determination of myoglobin in human heparinized or EDTA whole blood and plasma.

3. Special conditions for use statement(s):

   For prescription use and point-of-care use.

4. Special instrument requirements:

   PATHFAST© Analyzer

I. Device Description:

The PATHFAST© CK-MB-II and Myo-II tests are supplied in reagent kits. Each kit contains sufficient materials for 60 determinations. The calibrator materials are included with the reagent kit and are available separately. Calibration kits and diluent kits are also provided separately.

PATHFAST CK-MB-II reagent kit

Component	Quantity
Reagent Cartridge	6 cartridges x 10 trays
Calibrator 1	2 vials
Calibrator 2	2 vials
Calibrator diluent	4 vials of 1.0 mL each

Reagent Cartridge: The reagent cartridge contains 16 wells. Wells 1, 6, 8, 9, 10, 12, 14, 15, 16 are empty. The other wells are filled with the following reagents:

Contents of the PATHFAST CK-MB-II reagent cartridge

Reagent Description	Volume	Cartridge Well
Alkaline phosphatase (calf intestine) conjugated anti CK-BB monoclonal antibody (mouse) in MES buffer (pH 6.0) with 0.007% zinc chloride, and 0.06% sodium azide as preservative	50 µl	2
Washing Buffer: Tris buffer (pH 7.5) with 0.05% sodium azide as preservative	400 µl	3, 4, 5
Magnetic particles coated with anti CK-MB monoclonal antibody (mouse) in MOPS buffer	50 µl	7
Sample Dilution Buffer: Saline solution with BSA and 0.05% sodium azide as preservative	25 µl	11
Chemiluminescent substrate: CDP-Star	100 µl	13

Calibrator 1: Lyophilized preparation containing MOPS pH 7.2, lactose, enzyme free human serum, DTT, and Tween-20

Calibrator 2: Lyophilized preparation containing CK-MB, MOPS pH 7.2, lactose, enzyme free human serum, DTT, and Tween-20

Calibrator diluent: Aqueous solution with 0.05% sodium azide. For reconstituting Calibrators 1 and 2.

Contents of the PATHFAST Myo-II reagent kit

Component	Quantity
Reagent Cartridge	6 cartridges x 10 trays
Calibrator 1	2 vials of 1.0 mL each
Calibrator 2	2 vials of 1.0 mL each

Reagent Cartridge: The reagent cartridge contains 16 wells. Wells 1, 6, 8, 9, 10, 12, 14, 15, 16 are empty. The other wells are filled with the following

Contents of the PATHFAST Myo-II reagent cartridge

Reagent Description	Volume	Cartridge Well
Alkaline phosphatase (calf intestine) conjugated anti myoglobin monoclonal antibody (mouse) in MES buffer (pH 6.0) with 0.007% zinc chloride, and 0.06% sodium azide as preservative	50 µl	2
Washing Buffer: MES buffer (pH 7.5) with 0.05% sodium azide as preservative	400 µl	3, 4, 5
Magnetic particles coated with anti myoglobin monoclonal antibody (mouse) in MOPS buffer	50 µl	7
Sample Dilution Buffer: Saline solution with 0.05% sodium azide as preservative	25 µl	11
Chemiluminescent substrate: CDP-Star	100 µl	13

Calibrator 1: Tris pH 7.0 buffer containing, glycerol, BSA, and 0.05% sodium azide
Calibrator 2: Tris pH 7.0 buffer containing human myoglobin, glycerol, BSA, and 0.05% sodium azide

Contents of the PATHFAST CK-MB, and Myo Calibrator kits

Kit	**Component**	**Quantity**
CK-MB Calibrator Kit	Calibrator 1	2 vials
	Calibrator 2	2 vials
	Calibrator diluent	4 vials of 1.0 ml each
Myo Calibrator Kit	Calibrator 1	2 vials of 1.0 mL each
	Calibrator 2	2 vials of 1.0 mL each

Contents of the PATHFAST Sample Diluent 1 and 2 kits

Kit	**Component**	**Quantity**
Sample Diluent 1 Kit	Sample Diluent 1	2 vials of 20 mL each
Sample Diluent 2 Kit	Sample Diluent 2	2 vials of 20 mL each

PATHFAST Sample Diluent 1: Saline solution with < 0.1% sodium azide. For dilution of samples over the reportable range of the CK-MB-II and Myo-II test.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Stratus CS CK-MB and MYO TestPak

2. Predicate K number(s):

   k051650, k033487, k984093, k981098, k984067, k981099, k984065, k991102.

3. Comparison with predicate:

Similarities		
Item	Device	Predicates
Intended Use	Aid in the diagnosis of acute myocardial infarction. For use in clinical laboratory or point of care (POC) settings.	Same.
Storage	2-8 C	2-8 C
Calibration Levels	6	6
Barcode	Yes	Yes

Differences		
Item	Device	Predicate
Methodology	Chemiluminescent enzyme immunoassay	Solid phase radial partition immunoassay
Indications for use	Not for risk stratification	Risk stratification use.
Sample Types	Whole blood and Heparized Plasma	Heparinized Plasma
Range	CK-MB: 1- 250 ng/mL Myo: 5 -1000 ng/mL	CK-MB: 0- 150 ng/ml Myo: 0 -900 ng/mL

K. Standard/Guidance Document Referenced (if applicable):

CLSI EP5-A2: *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition.*

CLSI EP6-A: *Evaluation of the Linearity of Quantitative Measurement Procedures*: *A Statistical Approach; Approved Guideline.*

CLSI EP9-A2. *Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline—Second Edition.*

CLSI EP17-A: *Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline.*

CLSI C28-A2: *How to Define and Determine Reference Intervals in the Clinical Laboratory; Approved Guideline - Second Edition.*

ISO 17511:2003(E). *In vitro diagnostic medical devices—Measurement of quantities in biological samples—Metrological traceability of values assigned to calibrators and control materials*

ISO 14971:2000 *Medical devices - Application of risk management to medical devices*
ISO 13485:2003 *Medical devices - Quality management systems – Requirements for regulatory purposes*

L. Test Principle:

The PATHFAST CK-MB-II, and Myo-II tests are chemiluminescent enzyme immunoassays performed on the PATHFAST instrument.

Patient samples, whole blood or plasma, are dispensed by the operator into the designated area on the reagent cartridge. The instrument combines the patient sample, the antibody coated magnetic particles, and the alkaline phosphatase conjugate and incubates the mixture for 5 minutes at 37°C. During this incubation, the analyte in the patient sample binds to the antibody on the coated particles, and the alkaline phosphatase conjugate binds to the analyte-antibody coated-particle.

After the incubation, the instrument performs Bound/Free (B/F) separation using Magtration technology to remove any excess unbound reagents. The chemiluminescent substrate is then added. The substrate is catalyzed by the bound alkaline phosphatase, which results in emission of photons.

The photo-multiplier tube in the PATHFAST instrument detects the photons that are emitted during the reaction. The chemiluminescent count is converted to analyte concentration values by the instrument based on the master calibration curve for the reagent lot.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

CK-MB

Precision was assessed with Li-heparinized plasma and one whole blood, each at four levels. Each sample was tested 20 consecutive times and the intra-assay results are shown below.

Li-heparinized samples	**Level 1**	**Level 2**	**Level 3**	**Level 4**
Mean (ng/ml)	2.55	9.56	63.7	165
SD	0.134	0.380	2.16	5.38
%CV	5.2%	4.0%	3.4%	3.3%
Minimum	2.35	8.62	58.0	154
Maximum	2.84	10.2	66.7	178

Whole Blood samples	Level 1	Level 2	Level 3	Level 4
Mean (ng/ml)	2.76	9.52	60.7	175
SD	0.173	0.419	1.51	6.26
%CV	6.3%	4.4%	2.5%	3.6%
Minimum	2.49	8.80	57.7	154
Maximum	3.32	10.3	62.8	181
Range	0.83	1.50	5.1	27

Inter-assay precision was assessed with lithium heparinized plasma samples at three levels of the test range. The samples were tested in duplicate one a day for 20 days. The SD and %CV's for each level are shown in the table below.

Mean (ng/ml)	SD	CV
CK-MB Conc. of 2.69		
Within-run imprecision	0.147	5.4%
Total imprecision	0.225	8.4%
CK-MB Conc. of 36.0		
Within-run imprecision	1.42	3.9%
Total imprecision	2.29	6.4%
CK-MB Conc. of 211		
Within-run imprecision	6.76	3.2%
Total imprecision	14.6	6.9%

Myoglobin

Precision was assessed with Li-heparinized plasma and whole blood samples, each at four levels. Each sample was tested 20 consecutive times and the intra-assay results are shown below.

Li-heparinized samples	Level 1	Level 2	Level 3	Level 4
Mean (ng/ml)	42.0	131	276	826
SD	1.95	4.91	7.99	18.3
%CV	4.6%	3.8%	2.9%	2.2%
Minimum	37.7	125	263	795
Maximum	46.3	145	289	859
Whole Blood Samples	**Level 1**	**Level 2**	**Level 3**	**Level 4**
Mean (ng/ml)	42.2	111	250	859
SD	2.29	4.66	7.46	25.4
%CV	5.4%	4.2%	3.0%	3.0%
Minimum	36.8	104	235	814
Maximum	45.1	125	262	917

Inter-assay precision was assessed with lithium heparinized plasma samples at three levels of the test range. The samples were tested in duplicate one a day for 20 days. The SD and %CV's for each level are shown in the table below.

Mean (ng/ml)	**SD**	**CV**
Myo Conc. of 33.8		
Within-run imprecision	1.01	3.0%
Total imprecision	1.45	4.3%
Myo Conc. of 102		
Within-run imprecision	2.85	2.8%
Total imprecision	3.86	3.8%
Myo Conc. of 688		
Within-run imprecision	9.31	1.4%
Total imprecision	16.8	2.4%

Point of care precision studies

Precision studies were performed externally at 3 point of care sites by physician assistants and medical office personnel to support the device's point of care claim.

Testing was performed at the three sites with 6 trained users (2 different operators for each POC site). Precision testing was conducted using 2 levels of control for each analyte (run in duplicate) and with whole blood samples for 5 days per site. The following tables summarize the combined day to day and site to site results.

CK-MB				
Level 1				
	Site 1	Site 2	Site 3	Overall
Mean ng/mL	2.48	2.40	2.33	2.40
SD	0.121	0.171	0.090	0.142
% CV	4.9	7.1	3.9	5.9
Level 2				
	Site 1	Site 2	Site 3	Overall
Mean ng/mL	72.9	72.5	73.5	73.0
SD	2.41	3.37	246	2.71
% CV	3.3	4.6	3.3	3.7
Myoglobin				
Level 1				
	Site 1	Site 2	Site 3	Overall
Mean ng/mL	40.7	36.6	36.5	37.9
SD	4.24	3.58	2.98	4.04
% CV	10.4	9.8	8.2	10.7

Level 2				
	Site 1	Site 2	Site 3	Overall
Mean ng/mL	274	262	261	265
SD	22.0	14.1	16.2	18.1
% CV	8.0	5.4	6.2	6.8

Precision studies were conducted with lithium heparin whole blood samples. Ten samples were tested in duplicate. In order to obtain a normal and abnormal level, some normal samples were spiked with control materials to obtain samples at elevated levels. The table below shows the results from all three sites.

CK-MB results with whole blood samples					
Site 1					
Sample	**Rep 1**	**Rep 2**	**Mean**	**SD**	**CV**
WB1	16.5	16.7	16.6	0.141	0.9%
WB2	103	101	102	1.41	1.4%
WB3	5.61	5.71	5.66	0.071	1.2%
WB4	76.9	78.5	77.7	1.13	1.5%
WB5	22.1	20.8	21.5	0.919	4.3%
WB6	21.6	22.1	21.9	0.354	1.6%
WB7	39.3	39.9	39.6	0.424	1.1%
WB8	147	142	145	3.54	2.4%
WB9	246	235	241	7.78	3.2%
WB10	15.3	16.4	15.9	0.778	4.9%
Site 2					
Sample	**Rep 1**	**Rep 2**	**Mean**	**SD**	**CV**
WB11	184	177	181	4.95	2.7%
WB12	64.9	64.0	64.5	0.636	1.0%
WB13	11.1	10.6	10.9	0.354	3.3%
WB14	223	205	214	12.7	5.9%
WB15	104	108	106	2.83	2.7%
WB16	6.29	6.15	6.22	0.099	1.6%
WB17	151	154	153	2.12	1.4%
WB18	20.4	18.7	19.6	1.20	6.1%
WB19	42.9	45.0	44.0	1.48	3.4%
WB20	21.5	21.4	21.5	0.071	0.3%
Site 3					
Sample	**Rep 1**	**Rep 2**	**Mean**	**SD**	**CV**
WB21	58.6	62.1	60.4	2.47	4.1%
WB22	209	208	209	0.707	0.3%
WB23	47.3	45.9	46.6	0.990	2.1%

WB24	3.54	3.52	3.53	0.014	0.4%
WB25	79.4	79.5	79.5	0.071	0.1%
WB26	5.16	5.42	5.29	0.184	3.5%
WB27	99.8	96.3	98.1	2.47	2.5%
WB28	185	184	185	0.707	0.4%
WB29	11.1	11.3	11.2	0.141	1.3%
WB30	117	123	120	4.24	3.5%

Myoglobin results with whole blood samples

Site 1					
Sample	**Rep 1**	**Rep 2**	**Mean**	**SD**	**CV**
WB1	39.8	40.4	40.1	0.424	1.1%
WB2	792	778	785	9.90	1.3%
WB3	785	799	792	9.90	1.2%
WB4	124	135	130	7.78	6.0%
WB5	29.9	29.7	29.8	0.141	0.5%
WB6	167	148	158	13.4	8.5%
WB7	153	166	160	9.19	5.8%
WB8	688	687	688	0.707	0.1%
WB9	74.8	81.1	78.0	4.45	5.7%
WB10	46.8	45.4	46.1	0.990	2.1%
Site 2					
Sample	**Rep 1**	**Rep 2**	**Mean**	**SD**	**CV**
WB11	68.5	75.4	72.0	4.88	6.8%
WB12	17.9	18.4	18.2	0.354	1.9%
WB13	815	837	826	15.6	1.9%
WB14	528	538	533	7.07	1.3%
WB15	47.1	46.3	46.7	0.566	1.2%
WB16	332	343	338	7.78	2.3%
WB17	97.8	98.8	98.3	0.707	0.7%
WB18	447	440	444	4.95	1.1%
WB19	345	320	333	17.7	5.3%
WB20	577	628	603	36.1	6.0%
Site 3					
Sample	**Rep 1**	**Rep 2**	**Mean**	**SD**	**CV**
WB21	346	357	352	7.78	2.2%
WB22	262	255	259	4.95	1.9%

WB23	87.9	92.1	90.0	2.97	3.3%
WB24	478	494	486	11.3	2.3%
WB25	175	180	178	3.54	2.0%
WB26	652	677	665	17.7	2.7%
WB27	105	106	106	0.707	0.7%
WB28	74.7	77.5	76.1	1.98	2.6%
WB29	45.3	51.2	48.3	4.17	8.6%
WB30	690	672	681	12.7	1.9%

b. Linearity/assay reportable range:

CK-MB

The measuring range was assessed in a recovery study. CK-MB antigen purified from human heart was spiked into normal human lithium heparinized plasma. A dilution series was prepared by mixing two samples (samples A and B) of concentrations 264 and .686 ng/mL. Samples were run in triplicate on the PATHFAST instrument and the mean values were obtained and compared to the theoretical value to determine percent recovery. The results are shown in the table below for the range of (.686 to 264 ng/mL). The reportable range of the CKMB assay is 1 to 250 ng/mL.

Sample A ratio	**Sample B ratio**	**Theoretical Conc.** (ng/ml)	**Actual Conc.** (ng/ml)	**% Recovery**
0.0	1.0	.686	.686	100
0.1	0.9	26.3	27.0	97.4
0.2	0.8	52.0	53.3	97.6
0.3	0.7	73.9	79.7	92.7
0.4	0.6	100	106	94.3
0.5	0.5	125	132	94.7
0.6	0.4	149	159	93.7
0.7	0.3	174	185	94.1
0.8	0.2	213	211	100.9
0.9	0.1	236	238	99.2
1.0	0.0	264	264	100

A hook effect study was conducted to assess samples above the range of the test. Samples were prepared by spiking CK-MB antigen purified from human heart muscle into a buffer solution to 19452 ng/ml. Serial dilutions were prepared with buffer solution. Theoretical concentrations of CK-MB in the sample were calculated from the initial concentration of the spiked sample and the dilution factor. The sponsor reports that samples between 250 ng/ml to 19452 ng/ml return results above the range of the test.

Myoglobin

The measuring range was assessed in a recovery study. Myoglobin antigen purified from human heart was spiked into normal human lithium heparinized plasma. A dilution series was prepared by mixing two samples (samples A and B) with concentrations of 1041 and 2.25 ng/mL. Samples were run in triplicate on the PATHFAST instrument and the mean values were obtained and compared to the theoretical value to determine percent recovery. The results are shown in the table below for the range of (2.25 to 1041 ng/mL). The reportable range of the myoglobin assay is 5 to 1000 ng/mL.

Sample A ratio	**Sample B ratio**	**Theoretical Conc.** (ng/ml)	**Actual Conc.** (ng/ml)	**% Recovery**
0.0	1.0	2.25	2.25	100
0.1	0.9	101	106	95.3
0.2	0.8	194	210	92.4
0.3	0.7	288	314	91.7
0.4	0.6	381	418	91.1
0.5	0.5	475	522	91.0
0.6	0.4	569	626	909
0.7	0.3	699	729	95.9
0.8	0.2	817	833	98.1
0.9	0.1	932	937	99.5
1.0	0.0	1041	1041	100

A hook effect study was conducted to assess samples above the range of the test. Samples were prepared by spiking Myoglobin antigen purified from human heart muscle into a buffer solution to 107850 ng/ml. Serial dilutions were prepared with buffer solution. Theoretical concentrations of myoglobin in the sample were calculated from the initial concentration of the spiked sample and the dilution factor. The sponsor reports that samples between 1000 ng/ml to 107850 ng/ml return results above the range of the test.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Traceability

CK-MB is traceable to an IFCC standard. There is no recognized standard for myoglobin. The primary calibrators are used to determine the concentration of the master calibrators that are prepared in house. The master calibrator's concentrations are verified using three PATHFAST instruments calibrated with the primary calibrators. The master calibrators are used to determine the concentration of the stock solutions for the working calibrators. The stock solution for the working calibrators are prepared in the same manner

previously described. The working calibrators are prepared by diluting the stock solution to six specified levels of each test. Working calibrators are used to determine the concentration of the product calibrators. Concentrations are verified using three PATHFAST instruments calibrated with working calibrators. The product calibrators are prepared at two levels for each test. The CK-MB calibrators are provided in lyophilized form, while myoglobin calibrators are provided in liquid form.

	CK-MB	Myoglobin
Form	Lyophilized	Liquid
Level 1	0 ng/mL	0 ng/mL
Level 2	147 ng/mL	500 ng/mL

Stability

Three levels of three lots of CK-MB and myoglobin were run in triplicate monthly for 13 months to evaluate the assay's stability. The sponsor's results support their claim of 12 month stability. The sponsor conducted open vial studies for the calibrators after reconstitution with the calibrator diluent. Reconstituted calibrators are stable for 3 days at 2-8 C and one month at -20 C or lower.

d. Detection limit:

Limit of the Blank (LOB) was tested and the results were calculated according to CLSI EP17-A. A human normal lithium-heparinized plasma sample was tested 60 consecutive times with the PATHFAST CK-MB II and Myo-II. The LoB was calculated parametrically as the mean + 1.65x SD which was 0.50 ng/mL for CK-MB, and 0.486 ng/mL for myoglobin. The LoB was also calculated non-parametrically as the 95^{th} percentile of the blank. The measurements were 0.051 ng/mL for CK-MB and 0.536 ng/mL for myoglobin.

Limit of Detection (LoD) was conducted with five low level Lithium-Heparinized plasma samples. The samples were tested in replicates of three for 7 days for troponin and replicates of four over 5 days for CK-MB and myoglobin. The limit of quantitation was derived from the LoD. The LoD was calculated parametrically as

$LoD = LoB + c_\beta SD_S$, where $c_\beta = 1.645/(1-1/(4 \times f))$

For CK-MB, the LoD = 0.050 + [1.645/(1-1/(4 x 95)] x 0.0338 = 0.106 ng/mL.

For myoglobin, the LoD = 0.486 + [1.645/(1-1/(4 x 95))] x 0.250 = 0.898 ng/mL.

The limit of quantitation, or level above which the %CV was ≤10% for CK-MB was 0.192 ng/mL.
The limit of quantitation, or level above which the %CV was ≤10% for myoglobin was 1.93 ng/mL.

e. Analytical specificity:

Samples with interfering endogenous substances (6 levels) in human Li-heparinized plasma samples were combined with plasma samples to produce three levels. CK-MB levels were approx. 10, 37, and 140 ng/ml. Myoglobin levels were approx. 122, 279 and 850 ng/ml. Samples were tested on the PATHFAST instrument. The measurement obtained was compared to the expected value, which is the value of the plasma samples with no interfering substances added. The sponsor defined noninterference as recovery within +/- 10%. No interference was observed with bilirubin-conjugated and free (60 mg/dL), hemoglobin (1000 mg/dL), lipemia (3000 FTU), rheumatoid factor (500 IU/mL) and triglyceride (1000 mg/dL) in both assays. The myoglobin assay had an interference with bilirubin-free form of 36 ng/dL. This is noted in the package myoglobin assay.

Cross reactivity was studied using potentially cross-reacting substances commercially purchased. The substances were added to a human normal Li-heparinized plasma samples free from CK-MB. Cross –reactivity was calculated as the apparent analyte concentrations divided by the working concentration of the cross-reactants. The results for the cross-reactivity studies are shown in the tables below.

Cross-reactant	Working concentration	Cross reactivity
CK-MM	50000 ng/mL	0.000%
CK-BB	5000 ng/mL	0.072%

An extensive list of other compounds were evaluated for interference and was found to have no significant interference as summarized in the table below.

Drug	Highest level tested	CK-MB concentration (ng/ml)	% recovery
Acetaminophen	20 mg/dL (1320 µmol/L)	14.2	99.8%
Acetylsalicylic	0.3 ng/mL (1.67 nmol/L)	14.5	102.3%

Acid			
Allopurinol	2.5 mg/dL (184 µmol/L)	14.5	102.1%
Ampicillin	5 mg/dL (143 µmol/L)	14.7	103.5%
Ascorbic Acid	3 mg/dL (170 µmol/L)	14.4	101.2%
Atenolol	1 mg/dL (37.6 µmol/L)	14.8	104.0%
Caffeine	10 mg/dL (515 µmol/L)	12.8	90.1%
Captopril	5 mg/dL (230 µmol/L)	14.0	98.8%
Dopamine	65 mg/dL (3.4 mmol/L)	14.4	101.2%
Erythromycin	20 mg/dL (273 µmol/L)	13.7	96.5%
Furosemide	2 mg/dL (61 µmol/L)	14.1	99.3%
Methyldopa	2.5 mg/dL (118 µmol/L)	14.9	105.2%
Niphedipine	6 mg/dL (173 µmol/L)	14.4	101.2%
Phenytoin	10 mg/dL (396 µmol/L)	13.9	97.9%
Theophylline	25 mg/dL (1390 µmol/L)	13.6	95.5%
Verapamil	16 mg/dL (0.33 µmol/L)	13.3	93.4%
No interferent added		14.2	-
Digoxin	5 ng/mL (6.4 nmol/L)	12.1	98.6%
No interferent added (for digoxin interference)		12.2	-

Drug	**Highest level tested**	**Myo concentration (ng/ml)**	**% recovery**
Acetaminophen	20 mg/dL (1320 µmol/L)	169	97.9%
Acetylsalicylic Acid	0.3 ng/mL (1.67 nmol/L)	166	96.3%
Allopurinol	2.5 mg/dL (184 µmol/L)	167	96.7%
Ampicillin	5 mg/dL (143 µmol/L)	173	100.0%
Ascorbic Acid	3 mg/dL (170 µmol/L)	171	98.8%
Atenolol	1 mg/dL (37.6 µmol/L)	172	99.4%
Caffeine	10 mg/dL (515 µmol/L)	161	93.2%
Captopril	5 mg/dL (230 µmol/L)	166	96.1%
Digoxin	5 ng/mL (6.4 nmol/L)	159	92.1%
Dopamine	65 mg/dL (3.4 mmol/L)	162	93.6%
Erythromycin	20 mg/dL (273 µmol/L)	171	98.8%
Furosemide	2 mg/dL (61 µmol/L)	163	94.2%
Methyldopa	2.5 mg/dL (118 µmol/L)	163	94.2%
Niphedipine	6 mg/dL (173 µmol/L)	169	98.1%

Phenytoin	10 mg/dL (396 µmol/L)	159	92.1%
Theophylline	25 mg/dL (1390 µmol/L)	163	94.2%
Verapamil	16 mg/dL (0.33 µmol/L)	172	99.4%
No interferent added		173	-

f. Assay cut-off:

not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison analysis was performed with Li-heparinized plasma samples collected from patients who visited cardiovascular departments within hospitals. The samples were tested with the PATHFAST assay and the Stratus CS predicate assay.

CK-MB

Seventy-six Li-heparinized samples with values ranging from 1.30 to 242 ng/mL were tested. The resulting Passing and Bablok method equation was y=0.997x -0.423, r = 0.996.

Myoglobin

One hundred and twenty-six Li-heparinized samples with values ranging from 15 to 896 ng/mL were tested. The resulting Passing and Bablok method equation was y=1.00x + 1.16, r = 0.992.

Point of Care Method Comparison

Method comparison studies were performed externally by the POC sites by physician assistants and medical office personnel to support the device's point of care claim.

Testing was performed at three sites with 6 trained users (2 different operators for each POC site). Method comparison testing was conducted with 60 lithium heparin plasma samples (20 per site) previously tested with the predicate method tested using the PATHFAST tests.. The following table summarizes the Passing Bablok regression results.

Analyte	Sample range	Slope (ng/mL)	Confidence interval (ng/mL)	Intercept (ng/mL)	Confidence interval (ng/mL)	R
CK-MB	1.14 to 185	1.007	0.969-1.048	-0.274	-0.761-0.513	0.988
Myoglobin	22.1 to 851	1.046	1.023-1.073	5.535	0.373 to 9.981	0.996

b. Matrix comparison:

The sponsor conducted a matrix study to compare whole blood samples that were collected from patients in lithium heparin, sodium heparin, EDTA-Na and EDTA-K tubes. Plasma samples were prepared from each whole blood sample and were tested on the PATHFAST tests. CK-MB lithium heparin plasma samples (n=68) ranged from 0.237 to 232 ng/mL. Myoglobin lithium heparin plasma samples (n=67) ranged from 16.8 to 924 ng/mL. The results in the tables below show acceptable correlation between lithium heparin plasma and other matrices.

CK-MB	**N**	**Slope (95% CI)**	**Intercept (95% CI)**	**r**
Li-Heparin WB (y) vs. Li-Heparin Plasma (x)	68	0.984 (0.961 to 1.009)	0.007 (-0.100 to 0.125)	0.990
Na-Heparin Plasma (y) vs. Li-Heparin Plasma (x)	68	1.004 (0.988 to 1.020)	0.004 (-0.242 to 0.075)	0.998
Na-Heparin WB (y) vs. Li-Heparin Plasma (x)	68	0.964 (0.951 to 0.993)	0.009 (-0.126 to 0.096)	0.993
EDTA-2Na Plasma (y) vs. Li-Heparin Plasma (x)	68	1.027 (1.012 to 1.037)	0.043 (-0.077 to 0.132)	0.998
EDTA-2Na WB (y) vs. Li-Heparin Plasma (x)	68	1.010 (0.991 to 1.039)	0.040 (-0.047 to 0.205)	0.990
EDTA-2K Plasma (y) vs. Li-Heparin Plasma (x)	68	1.019 (1.006 to 1.034)	0.062 (-0.020 to 0.163)	0.996
EDTA-2K WB (y) vs. Li-Heparin Plasma (x)	68	1.006 (0.990 to 1.045)	0.058 (-0.035 to 0.198)	0.991

Myoglobin	N	Slope (95% CI)	Intercept (95% CI)	r
Li-Heparin WB (y) vs. Li-Heparin Plasma (x)	67	0.967 (0.937 to 1.000)	0.210 (-2.070 to 4.225)	0.993
Na-Heparin Plasma (y) vs. Li-Heparin Plasma (x)	67	1.009 (0.990 to 1.032)	0.825 (-2.176 to 4.245)	0.996
Na-Heparin WB (y) vs. Li-Heparin Plasma (x)	67	0.957 (0.924 to 0.991)	1.394 (-0.631 to 6.415)	0.994
EDTA-2Na Plasma (y) vs. Li-Heparin Plasma (x)	67	1.002 (0.980 to 1.021)	-0.543 (-2.793 to 3.643)	0.995
EDTA-2Na WB (y) vs. Li-Heparin Plasma (x)	67	0.968 (0.940 to 0.997)	1.769 (-1.580 to 5.168)	0.992
EDTA-2K Plasma (y) vs. Li-Heparin Plasma (x)	67	0.997 (0.975 to 1.017)	-0.116 (-3.678 to 1.915)	0.994
EDTA-2K WB (y) vs. Li-Heparin Plasma (x)	67	0.980 (0.948 to 1.014)	2.330 (-0.479 to 6.580)	0.991

3. Clinical studies:

   a. Clinical Sensitivity:

   Not applicable.

   b. Clinical specificity:

   Not applicable.

   c. Other clinical supportive data (when a. and b. are not applicable):

   Not applicable.

4. Clinical cut-off:

   Not applicable

5. Expected values/Reference range:

The sponsor conducted a reference range study for both analytes.

CK-MB

302 Li-heparinized plasma samples with values ranging from 0.116 to 4.59 ng/mL were collected from healthy volunteers and analyzed on the PATHFAST CK-MB-II assay. The sponsor's non-parametrical analysis represents the central 99th percentile of the population tested. The expected values for the 302 apparently healthy individuals is 0.189 to 3.01 ng/mL.

Myoglobin

198 Li-heparinized plasma samples with values ranging from 0.764 to 109 ng/mL were collected from healthy volunteers and analyzed on the PATHFAST Myo-II assay. The sponsor's non-parametrical analysis represents the central 99th percentile of the population tested. The expected values for the 198 apparently healthy individuals is 12.8 to 74.5 ng/mL

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.